

AMENDMENTS TO THE CLAIMS

A listing of all currently pending claims is provided and will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A method of ~~selection-selecting~~ and/or identifying at least one protein affinity ligand by inverse screening, wherein the affinity ligand ~~are antibodies, is an antibody~~ that binds to at least one target protein of interest, comprising the steps of:

(A) obtaining a ~~real or theoretical~~ first mass spectrometry based characterization of at least one target protein by ~~either:~~

- i. ~~—subjecting said at least one target protein to a mass spectrometry based method characterization; or~~
- ii. ~~—predicting the mass spectrometry based characterization from known data;~~

(B) utilizing said at least one target protein:

- i. ~~—generate at least one antibody thereto by immunization; and/or~~
- ii. to select, ~~using a single or multiple rounds of binding,~~ said at least one antibody thereto;

(C) screening said at least one antibody ~~generated in~~ of step B(i) and/or selected by step (B)(ii) by:

- i. adding one or more proteins including said at least one target proteins to at least one antibody of generated in step (B)(i) ~~or the at least one antibody selected in step (B)(ii), each said antibody~~ being used individually, and

ii. after removing any proteins which have not bound, eluting the at least one target protein that has bound to said antibody thereby providing at least one eluted target protein;

(D) obtaining a second mass spectrometry based characterization of said
subjecting the at least one eluted target protein to mass spectrometry
based characterization; and

(E) by comparing the said first mass spectrometry based characterization and
said second mass spectrometry based characterization of said eluted
target protein to characterization obtains in steps (A) and (D), selecting
and/or identifying determine said at least one antibody that binds to said
at least one target protein of interest.

2. (Currently Amended) A method as claimed in claim 1 wherein the at least one target protein has of interest have been previously resolved by 2D electrophoresis.

3. (Currently Amended) A method as claimed in claims 1 or 2 wherein between steps (B) and (C) the at least one antibody obtained in step (B)(i.) are is cloned.

4. (Currently Amended) A method as claimed in claim 1 wherein the at least one target proteins of interest are is present in a mixture of proteins.

5. (Previously Amended) A method as claimed in claim 1 wherein the method is a method for selecting and identifying at least one protein affinity ligand to at least one target proteins.

6. (Currently Amended) A method as claimed in claim 1 wherein the mass spectrometry based characterization further includes acquisition the use of sequence tag data.

7. (Currently Amended) A method as claimed in claim 1 wherein the ~~at least one~~ antibody ~~optionally generated in~~ of step (B)(i) is immobilized on a support comprising nitrocellulose or PVDF.

8. (Currently Amended) A method as claimed in claim 7 wherein the support ~~upon which the at least one antibody is immobilised and the nitrocellulose or PVDF~~ is are treated with an oligosaccharide or polyvinylpyrrolidone solution to block any remaining binding sites.

9. (Original) A method as claimed in claim 8 wherein the oligosaccharide is ficoll.

10-16. (Previously Canceled)

17. (Currently Amended) A method as claimed in claims 1, 2, 7, 8, or 9 wherein the first and second mass spectrometry based characterization is obtained by mass spectrometry.

18. (Currently Amended) A method as claimed in claims 1, 2, 7, 8, or 9 further comprising the use of automated high-throughput mass spectrometry.

19. (Currently Amended) A method as claimed in claim 2 wherein the ~~at least one~~ antibody ~~generated in~~ of step (B)(i) is immobilized on a support comprising nitrocellulose or PVDF.

20. (Currently Amended) A method as claimed in claim 19 wherein the support ~~upon which the at least one antibody is immobilized~~ is are treated with an oligosaccharide or polyvinylpyrrolidone solution to block any remaining binding sites.

21. (Previously Presented) A method as claimed in claim 20 wherein the oligosaccharide is ficoll.

22-27. (Previously Canceled)

28. (Currently Amended) A method as claimed in claim 2 wherein the at least one target proteins of interest ~~is~~ are present in a mixture of proteins.

29. (Currently Amended) A method as claimed in claim 2 wherein the method is a method for selecting and identifying protein affinity ligands to using a mixture ~~a plurality of~~ proteins.

30. (Currently Amended) A method as claimed in claim 2 wherein the ~~other~~ mass spectrometry based characterization includes the use ~~acquisition~~ of sequence tag data.

31. (Currently Amended) The method of claim 1 wherein said mass spectrometry based characterization is a peptide mass fingerprinting.

32-36. (Previously Canceled)

37. (Currently Amended) A method as claimed in claim 1 wherein an eluting agent is further provided for eluting said at least one target protein from antibody-protein complexes.

38. (Previously Presented) A method as claimed in claim 37 wherein the eluting agent is formic acid.

39. (Currently Amended) A method as claimed in claim 8 wherein an eluting agent is further provided for eluting said at least one target protein from antibody-protein complexes.

40. (Previously Presented) A method as claimed in claim 39 wherein the eluting agent is formic acid.

41. (Currently Amended) A method as claimed in claim 19 wherein an eluting agent is further provided for eluting said at least one target protein from antibody-protein complexes.

42. (Previously Presented) A method as claimed in claim 41 wherein the eluting agent is formic acid.

43. (Currently Amended) A method as claimed in claim 20 wherein an eluting agent is further provided for eluting said at least one target protein from antibody-protein complexes.

44. (Previously Presented) A method as claimed in claim 43 wherein the eluting agent is formic acid.

45. (Currently Amended) A method as claimed in claim 21 wherein an eluting agent is further provided for eluting said at least one target protein from antibody-protein complexes.

46. (Previously Presented) A method as claimed in claim 45 wherein the eluting agent is formic acid.

47. (New) A method as claimed in claim 1 wherein said at least one antibody is further generated by immunization.

48. (New) A method as claimed in claim 1 wherein said first mass based spectrometry characterization is theoretically determined based on the DNA sequencing of the corresponding gene.

49. (New) A method as claimed in claim 1 wherein the antibody is selected using single or multiple rounds of binding.